



# Abdominal obesity, hypertension, antihypertensive medication use and biochemical recurrence of prostate cancer after radical prostatectomy



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## KEYWORDS

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**Abstract Background:** The aim of this study was to determine whether abdominal obesity, including visceral adipose tissue (VAT) measured by computed tomography and blood pressure (BP) were associated with biochemical recurrence of prostate cancer after prostatectomy. **Methods:** We investigated 283 patients who underwent radical prostatectomy for prostate cancer retrospectively. We obtained information on body mass index (BMI), waist circumference (WC), VAT, BP, antihypertensive drug use, pretreatment prostate-specific antigen levels, pathological Gleason scores and postoperative surgical margin status. Hypertension was defined as systolic BP (SBP)  $\geq 130$  mmHg or diastolic BP  $\geq 85$  mmHg. **Results:** Among 283 patients, 41 (14%) developed biochemical recurrence subsequently. We performed a Cox proportional hazard regression analysis to assess the association of each obesity measurement and SBP with biochemical recurrence using clinical predictors as potential confounders. No association was observed between any obesity measurement assessed and biochemical recurrence. Adjusting for each of BMI, WC and VAT, a higher SBP was associated significantly with biochemical recurrence (hazard ratio [HR], adjusted for VAT = 1.04; 95% confidence interval [CI] = 1.02–1.07). Adjusting for obesity (BMI  $\geq 25$  kg/m<sup>2</sup>), hypertension was also associated significantly with biochemical recurrence (HR = 2.08; 95% CI = 1.09–3.97). Compared with normotensive patients, those with untreated and uncontrolled hypertension had a significantly increased risk of biochemical recurrence (HR = 2.45; 95% CI = 1.06–5.66).

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**Conclusions:** A higher BP and untreated, uncontrolled hypertension were independent risk factors for biochemical recurrence after prostatectomy. Control of hypertension could be an important treatment strategy for preventing biochemical recurrence.

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## 1. Introduction

Prostate cancer has become a major public health problem in many countries with increasingly ageing populations. Approximately 40% of those who choose definitive therapy will undergo radical prostatectomy [1]. Of the patients treated with radical prostatectomy, 15–33% experience biochemical recurrence [1–4].

Although the association between obesity and prostate cancer incidence has been inconsistent, obesity has been consistently associated with an increased risk of prostate cancer aggressiveness [5]. Obesity has been reported to be a risk factor for biochemical recurrence after radical prostatectomy [6–10], although some studies failed to find such an association [11–14]. Although obesity is often defined using body mass index (BMI) data, BMI is considered a suboptimal measure of abdominal obesity. Visceral adipose tissue (VAT), measured by computed tomography (CT), is considered to be a more accurate measure of abdominal obesity. However, little has been reported on any association between VAT and biochemical recurrence.

Hypertension has been reported to be associated with prostate cancer risk [15,16] and more aggressive tumour characteristics [17]. More recently, hypertension was shown to contribute to biochemical recurrence following radical prostatectomy [6,11]. In those previous studies, however, information on a history of hypertension was extracted from medical records instead of evaluating blood pressure (BP) measurements, limiting an accurate assessment of the impact of BP on biochemical recurrence. Furthermore, there is scant evidence to indicate whether antihypertensive medication use influences biochemical recurrence.

Because obesity and hypertension are found in substantial proportions of the ageing population, the associations between each of them and prostate cancer prognosis are of great clinical significance. Appropriate management of these modifiable lifestyle factors may help improve prostate cancer outcomes. Thus, we collected data regarding abdominal obesity, including BMI, waist circumference (WC), and VAT, and hypertension, including BP and antihypertensive medication use. The aims of this study were to determine whether abdominal obesity, including VAT measured by CT, and BP were associated with biochemical recurrence and to investigate the impact of antihypertensive medication use on biochemical recurrence.

## 2. Patients and methods

The study population consisted of a consecutive group of patients who were diagnosed with prostate cancer and underwent radical prostatectomy between December 2008 and December 2012. All patients were treated at the St. Luke's International Hospital. The diagnosis of primary adenocarcinoma of the prostate was confirmed histopathologically by the St. Luke's International Hospital Department of Pathology. No patient received preoperative radiation therapy or neoadjuvant androgen deprivation therapy. The St. Luke's International Hospital Internal Review Board approved all study procedures.

Basically, prostate-specific antigen (PSA) levels were checked postoperatively at 1–3 months, and then every 3 months thereafter with a median length of follow-up post-surgery of 30 months (2.5 years). PSA concentrations are generally expected to become undetectable within 4 weeks after prostatectomy [18]. Eight subjects were excluded because they did not reach a PSA nadir of  $\leq 0.2$  ng/mL within 3 months, suggesting some residual disease. We also excluded patients who had received adjuvant radiation therapy ( $n = 5$ ). Another patient was excluded for missing height data ( $n = 1$ ). Consequently, we included 283 patients in the analysis. No patient showed evidence of distant metastasis at the time of treatment and only one had regional lymph node involvement (histopathologically after lymph node sampling). Subjects were followed up from the time of surgery until the date of occurrence, loss to follow-up or the end of the study (29th January 2014).

Body weight and height were measured, and BMI was calculated as weight in kilograms divided by height in metres squared. A pelvic CT was routinely performed to confirm the presence or absence of metastasis. Body fat distribution was assessed by CT with a 10-mm-thick slice at the level of the umbilicus. The VAT and WC were assessed using commercially available software (Virtual Place, Rajjin; AZE Inc., Tokyo, Japan). VAT was defined as the area enclosed by the peritoneal membrane with attenuation for fat tissue, ranging from  $-190$  to  $-30$  Hounsfield units [19,20], and was measured semiautomatically. WC was calculated automatically.

Biochemical recurrence was defined as two consecutive rising detectable PSA concentrations of  $>0.2$  ng/mL [21]. Data extracted from medical records included height, weight, WC, VAT, BP, antihypertensive

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